Current Biology, Vol. 13, 585–589, April 1, 2003, ©2003 Elsevier Science Ltd. All rights reserved. DOI 10.1016/S0960-9822(03)00171-4

# Stimulus-Driven and Voluntary Saccades Are Coded in Different Coordinate Systems

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## Summary

**We make fast, "saccadic" eye movements to view our surroundings, "voluntary" saccades when saccade targets are deliberately selected, and "stimulus-driven" saccades when a target suddenly appears. Saccades of patients with spatial neglect have been studied to identify the coordinate systems guiding such behavior. However, previous reports disagree on whether neglect involves an eye-centered deficit of (delayed and hypometric) saccades specifically when performed in the direction opposite the brain lesion [1–5] or not [6–8]. We show that this inconsistency is due to independent mechanisms underlying voluntary and stimulus-driven saccades. We used a new experimental procedure comparing identical saccades performed either during an exploratory search task or a stimulus-driven task, both of which required similar cognitive functions (Figure 1). Only the patients' stimulus-driven saccades showed the eye-centered deficit. The same saccades were intact when voluntarily performed. However, here the patients showed a head-centered deficit; their saccades ignored the left part of space. In none of our control subjects with or without brain lesions did the neglect patients' pattern of deficits occur. The results argue that the brain flexibly uses a system of distinct but interrelated neural circuits for visual orienting to optimally encode its sensorimotor functions in multiple behavioral situations.**

## Results and Discussion

Neurological patients suffering from spatial neglect have trouble detecting or responding to stimuli contralateral to the side of the brain lesion. Here, we used a new test procedure to systematically study the neglect patients' eye movement deficits. The procedure comprised two cognitively similar tasks that allowed a direct comparison of voluntary saccades and of stimulus-driven saccades aimed at identical target locations that were either voluntarily selected or stimulus-driven. In the first part of the procedure, the *exploratory letter search task (task 1)*, subjects searched for the target letter "A" in a display and we recorded their "scanpaths," that is, the sequences of saccades and fixations (Figure 1A). In the second part of the procedure, the *stimulus-driven letter search task (task 2)*, the subjects observed a red square-shaped target window that jumped across the display and thereby revealed different letters, one at a time; the revealed letter was sometimes an "A." The displacements of the red target window matched the individual scanpath that the respective subject had performed during task 1 (Figure 1B). So, when the subjects tracked the jumps of the red target window with the eyes in task 2, they showed stimulus-driven saccades that had the same metrics as the voluntarily executed, exploratory saccades from task 1.

With this test procedure, we studied the eye movements of neglect patients (NEG) with right-brain damage. We also examined non-brain damaged subjects (NBD) and patients without neglect but with lesions either in the right brain (RBD) or in the left brain (LBD, see Experimental Procedures and Supplemental Data) as control subjects. Exclusion criteria were visual-field defects, oculomotor palsies, language deficits and reduced tonic alertness.

In the exploratory letter search task, the neglect patients showed the typical deficit of exploration [6–8, 10–13]. They explored the right half of the letter arrays but mostly ignored the left half. In contrast, the control subjects showed uniform distributions of saccades. This bias of the average horizontal eye fixation yielded a significant difference between neglect patients and control subjects (NEG: $+5.8°$, NBD: $-0.6°$, RBD: $-0.5°$, LBD: $-1.4°$; ANOVA: $F(3, 17) = 14.76$, $p < 0.001$; Scheffé tests NEG versus NBD/RBD/LBD: $p$'s $\leq 0.001$).

An eye-centered deficit of the single saccades would result from impaired processes either of saccade target selection or of saccade performance. So, saccades in the leftward direction would show smaller amplitudes than rightward saccades. Consequently, moving the eyes in the leftward direction would require more saccades than moving them rightward [1]. However, for task 1 we found neither the percentage of saccades nor saccade amplitude to show the expected asymmetry (Figure 2); ANOVAs yielded no significant subject group $\times$ saccade direction interaction. We observed only differences between horizontal (leftward *and* rightward) and vertical saccades or between upward and downward saccades (percentage of saccades: $F(1.1, 18.6) = 7.53$, $p = 0.012$; saccade amplitude: $F(1.7, 28.9) = 6.45$, $p = 0.007$; degrees of freedom were Greenhouse-Geisser corrected). Even the results from individual neglect patients showed no evidence for a direction-specific saccade deficit in task 1.

Furthermore, we could rule out the possibility that such a deficit might have arisen only farther on the contralesional side. To look at that, we binned the saccade data according to the saccades' start locations in one of four segments of the letter array (left, central left, central right, or right). With these data sets we calculated a series of additional ANOVAs similar to the ones above

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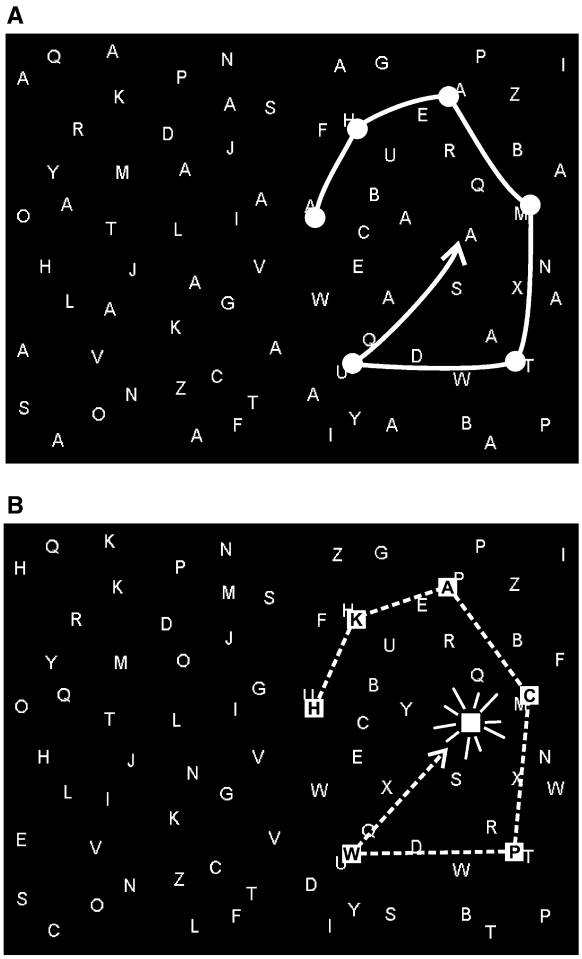


Figure 1. Experimental Paradigm

(A) Exploratory letter search task. Each subject explored six randomly distributed arrays of white letters on a black background and indicated each detected target letter "A" with a mouse click (48 or 60 stimuli, 8–24 target letters "A." Vertical size of letters: 0.7°. Height of array: 23°. Width: 30.5°. Presentation time per array: 30 s). Superimposed onto the display is a schematic of a short piece of a subject's scanpath consisting of fixations (white circles) and saccades (lines connecting the circles).

(B) Stimulus-driven letter search task. Individual scanpaths from task 1 were fed into a special presentation software that generated a red square-shaped target window (0.9° × 0.9°). The window should be visually tracked while it jumped across the letter arrays. During the experiment the target window was visible at one position at a time (here depicted as a white square with "light beams"). But for comparisons with (A), the graph also shows previous window positions. The displacements of the target window matched exactly the metrics of the scanpaths the subject had used during the searches in task 1 [9]. Every 3 s the window jumped to a new position (so that all subjects could track it). For the first 1.5 s the red window remained blank (to encourage maintained fixation) and then revealed randomly selected letters, one at a time (the probability of A's matched that of task 1). A's detected within the target window should be indicated by a mouse click (A's in the letter arrays in the background were replaced by distracter letters to avoid confusion).

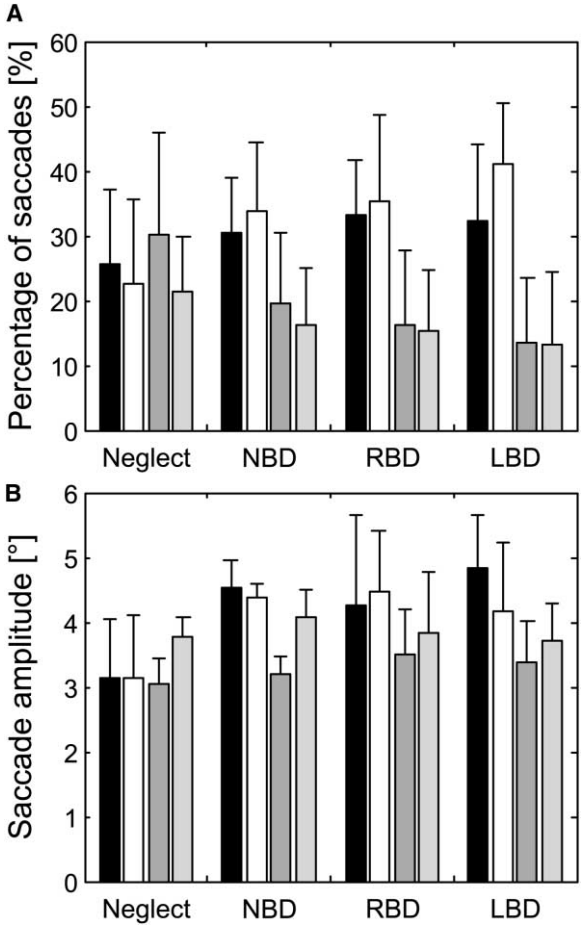


Figure 2. Parameters of Saccades Performed during the Exploratory Letter Search Task

(A) Percentage of saccades and (B) saccade amplitude performed in leftward (black bars), rightward (white bars), upward (dark gray bars), or downward directions (light gray bars) for the four subject groups separately.

but with a third independent variable, "spatial segment." Additionally, we used a somewhat different data analysis to calculate leftward-rightward ratios from the saccade parameters [12]. However, none of these analyses yielded evidence for a direction-specific saccade deficit (see Supplemental Data available with this article online for details).

In contrast, in the second, stimulus-driven letter search task, we observed a prominent direction-specific deficit in the neglect patients' saccades. When tracking the jumping target window in the leftward direction, the neglect patients performed more saccades than in any other direction (Figure 3A), and they showed smaller saccade amplitudes. Accordingly, ANOVAs yielded significant subject group × saccade direction interactions (saccade numbers: $F(6.9, 39.1) = 6.40$, $p < 0.001$; saccade amplitude: $F(6.5, 37.0) = 3.75$, $p = 0.04$). Subsequent group-wise ANOVAs found these results to be due to significant differences in the neglect patients (saccade numbers: $F(1.4, 4.3) = 11.72$, $p = 0.021$; saccade amplitude: $F(2.0, 5.9) = 18.11$, $p = 0.003$) but not in the control groups. Moreover, *all* our neglect patients performed more saccades of smaller amplitude when tracking the red target window jumping in the leftward direction versus any other direction (Mann-Whitney U tests of leftward versus rightward saccades: $p \leq 0.035$).

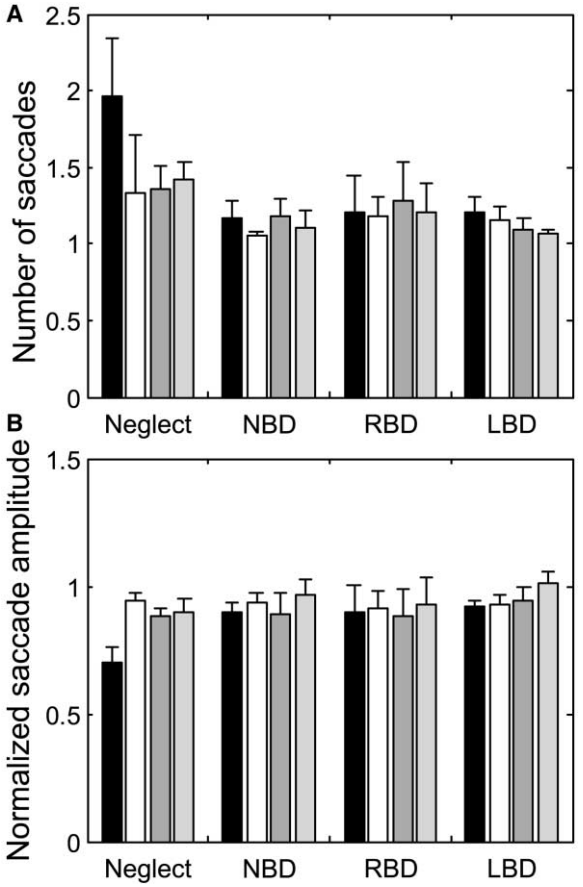


Figure 3. Parameters of Saccades Performed during the Stimulus-driven Letter Search Task

(A) Average number of saccades performed to track the target window jumping in leftward (black bars), rightward (white bars), upward (dark gray bars), or downward direction (light gray bars) for the four subject groups separately.

(B) Average normalized saccade amplitude performed to track a target jump (i.e., saccade amplitudes were divided by the size of the respective jump of the target window to correct for inter-individual differences from task 1).

Only one patient without neglect (RBD8) exhibited a similar pattern of leftward-rightward differences ($p$'s $<$ 0.001). However, this deficit was not restricted to the leftward direction; RBD8 showed similar differences for upward versus rightward target jumps ($p$'s $\leq$ 0.015) with no evidence for more disturbed saccades aimed up and left rather than up and right.

This direction-specific saccade deficit cannot be attributed to motor problems. The locations of the saccadic targets in task 2 were identical to the target locations self-chosen by each subject in task 1, so any deficit downstream in the saccade system would have shown up in both tasks. Also, both tasks required similar letter detection mechanisms. Therefore, it appears unlikely that differences in cognitive load caused the neglect patients to perform differently in the two tasks. The second task did differ from the first in that it presented a salient saccade goal and provided more time to perform each saccade. However, both of these differences should have made the task easier. Therefore, it is not clear how they could have caused the observed direction-specific saccadic deficit. Instead, it can be concluded that the direction-specific saccadic deficit in neglect patients predominantly occurs with stimulus-driven eye movements performed in the contralesional direction. In contrast, the neglect patients' voluntary saccades during visual search can be unaffected by an eye-centered deficit. These results reconcile previous, allegedly conflicting, findings reporting either direction-specific deficits in the saccades of neglect patients [1–5] or intact saccades [6–8].

Strikingly, however, another deficit became obvious in the neglect patients' exploratory saccades. That is, the spatial distribution of these saccades exhibited the typical ipsilesional bias of exploration (e.g., [6–8, 10–13]), reflecting disrupted spatial coding of saccades during visual search. (This deficit may be further aggravated by a disturbed memory of prefixated stimuli [8]. However, a disrupted memory is a nonspatial problem that cannot explain the ipsilesional search bias itself.) Thus, in addition to the eye-centered deficit in stimulus-driven saccades, we found an impairment of exploratory saccades in head-centered coordinates (trunk-centered coordinates could not be tested in the present experimental setup but are known to be affected in neglect, e.g., [13]).

There is evidence that such body-centered reference frames are also associated with stimulus-driven saccades; the direction-specific deficit worsens when neglect patients begin their saccades from fixations farther on the left as opposed to on the right side of space [2, 3]. However, when we examined whether the neglect patients' number of stimulus-driven saccades or these saccades' amplitudes varied with spatial coordinates, we did not spot any linear or nonlinear influences for the range of fixation locations tested in the present study. So, body-centered coordinates may be involved in the deficit of stimulus-driven saccades, but they are less important than eye-centered coordinates, and this is opposite to what we found for the neglect patients' deficit during exploration.

The two distinct deficits argue for different neural mechanisms participating in the generation of stimulus-driven and voluntary saccades, which confirms previous data [14–25]. However, obviously the independence between stimulus-driven and voluntary saccade generation must be limited. At some point, the two systems merge on the way to the brainstem, and functional imaging studies suggest that, in part, this takes place even on the level of cortical networks [26–30].

Because spatial neglect can be regarded as a "breakdown" of partly the same neural circuits or of circuits closely connected with these networks, it is no surprise that neglect is correlated with disturbed stimulus-driven as well as with disturbed voluntary functions [6, 10, 31]. In agreement with these data, all of our neglect patients—but no control subjects—showed impairments of stimulus-driven as well as of voluntary saccades, despite considerable differences in brain lesions and in recovery time.

A close link between an eye-centered deficit and a head-centered deficit corresponds to the notion of a close relation of eye-centered and head-centered representations of space as suggested by different models.

The "gain-field model" assumes that body-centered coordinates are implicitly represented in assemblies of neurons with eye-centered receptive fields [32]. The "conversion on command model" [33] suggests that the brain initially represents a target in eye-centered coordinates and later converts them into the respective coordinate system that is appropriate for a particular task. Accordingly, a suddenly appearing target eliciting a stimulus-driven saccade would be sufficiently represented in eye-centered coordinates. In contrast, visual search requires representations that keep track of spatial relations across eye movements and thus directly or indirectly generate information about head-centered coordinates.

A close relation between deficits of stimulus-driven saccades and those of exploratory saccades does not imply that both deficits *always* occur together. For instance, direction-specific saccade deficits arise with hemianopia and disrupt the visual input into the cortex [1, 34]. Similarly, a disturbed cortical output to subcortical structures might result in a direction-specific deficit but no deficit of visual search. One example is presumably patient RBD8, tested in the present study. Other examples seem to be patients with lesions in the posterior limb of the internal capsule [35]. Finally, left-brain damage seldom causes neglect. Therefore, left hemisphere lesions are most likely not associated with disturbed visual search. However, they can lead to direction-specific deficits in stimulus-driven saccades [19]. In contrast, in the right hemisphere, deficits in the spatial distribution of visual search should be yoked to a direction-specific deficit of stimulus-driven saccades. Is this always the case? To our knowledge, there is only one study finding no relation between neglect and disrupted contralesional stimulus-driven saccades [36]. However, stimulus-driven saccades were examined with a temporal gap between the offset of the fixation point and the onset of the target stimulus. It is now known that this "gap paradigm" can significantly reduce the direction-specific deficit in neglect [4].

Our study yields new insights into the coordinate systems that guide spatial behavior, a major issue in understanding the brain's sensorimotor functions. Our results suggest that stimulus-driven and exploratory saccades are generated in a system of neural circuits that operates in different spatial coordinates, as required in a multitude of situations. What is more, the correlation between the observed saccade deficits and neglect suggests that this system is also involved in more general functions of visual orienting, consistent with the strong association of eye movements and attentional mechanisms [37–40].

## Experimental Procedures

All subjects gave their informed consent to participate in this study, which was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. We tested four patients with right-brain damage and spatial neglect and four age-matched non-brain-damaged subjects. Two additional control groups comprised brain-damaged patients without any symptoms of neglect, nine patients with right-brain damage and four patients with left-brain damage. As revealed with standard neurological examination, none of the patients showed visual-field deficits (for clinical and demographic data of the brain-damaged patients, see Supplemental Data). For details concerning test analysis and criteria used for the diagnosis of neglect, see [41].

During the experiment, the subjects sat in a dimly lit room in front of a computer monitor. A head and chin rest stabilized the head. Eye movements were recorded with a video-oculographic system (3D VOG, SMI, Berlin, sampling rate: 50 Hz).

## Supplemental Data

For clinical and demographic information about patients and further analyses of experimental data, see the Supplemental Data available with this article online at http://images.cellpress.com/supmat/supmatin.htm.

## Acknowledgments

This work was supported by grants from the Deutsche Forschungsgemeinschaft (KA 1258/2-3, SFB 550-A4). We thank Igor Frenkel, Jonathan J. Marotta, and Douglas B. Tweed for helpful comments on the manuscript.

Received: December 16, 2002
Revised: January 23, 2003
Accepted: February 4, 2003
Published: April 1, 2003

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